Lyme disease and Pregnancy

Epidemiology and Pathobiology of *Borrelia*: Implications for Research

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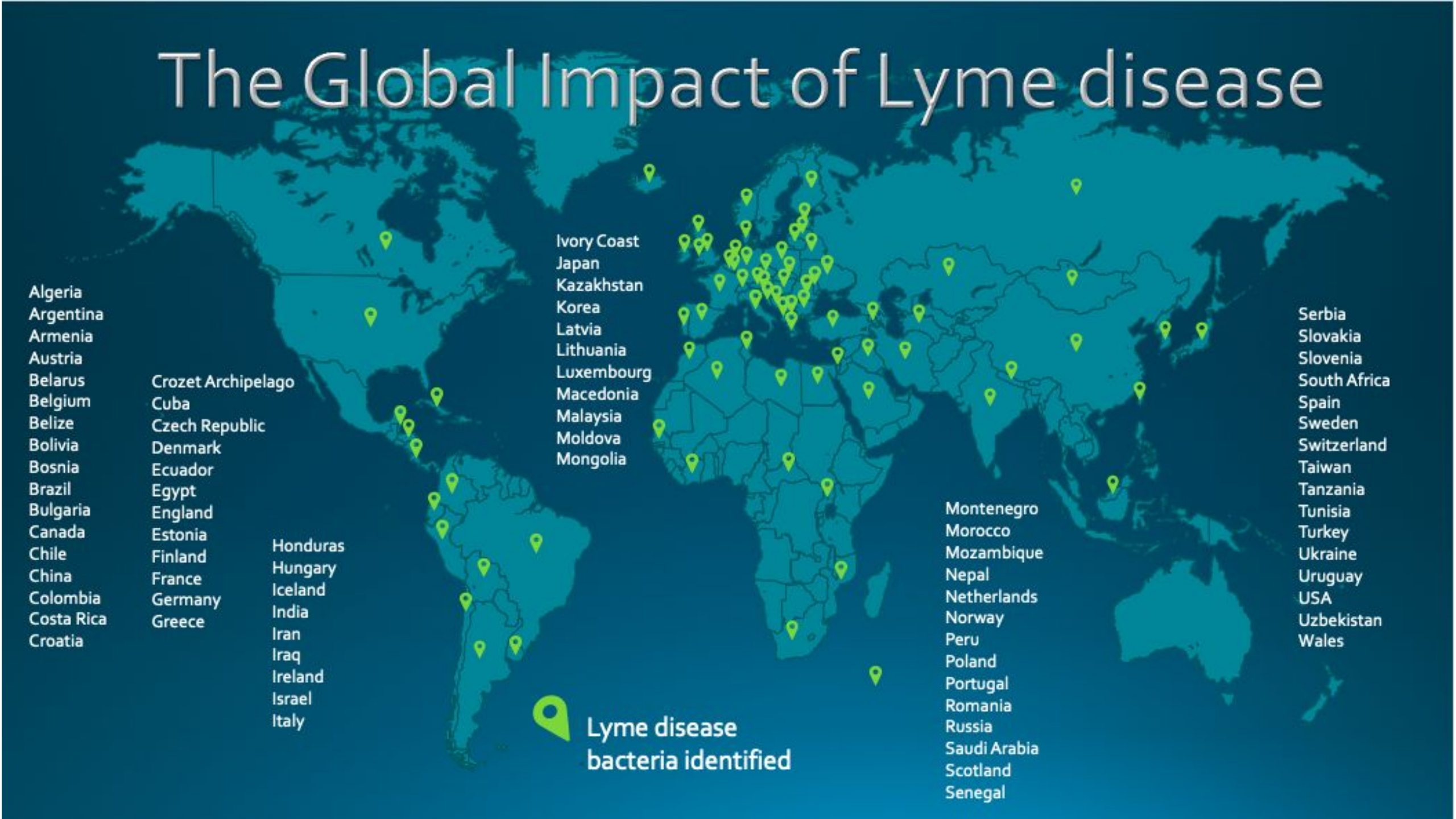
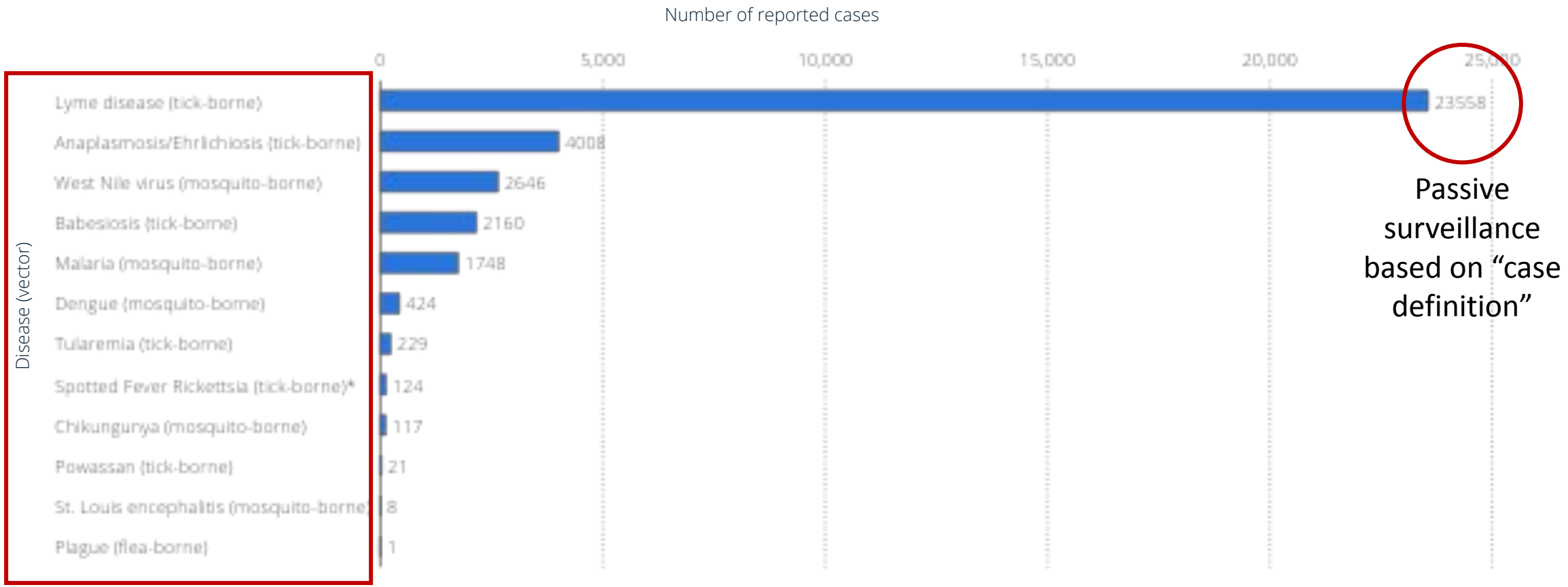
Mom

The Global Impact of Lyme disease



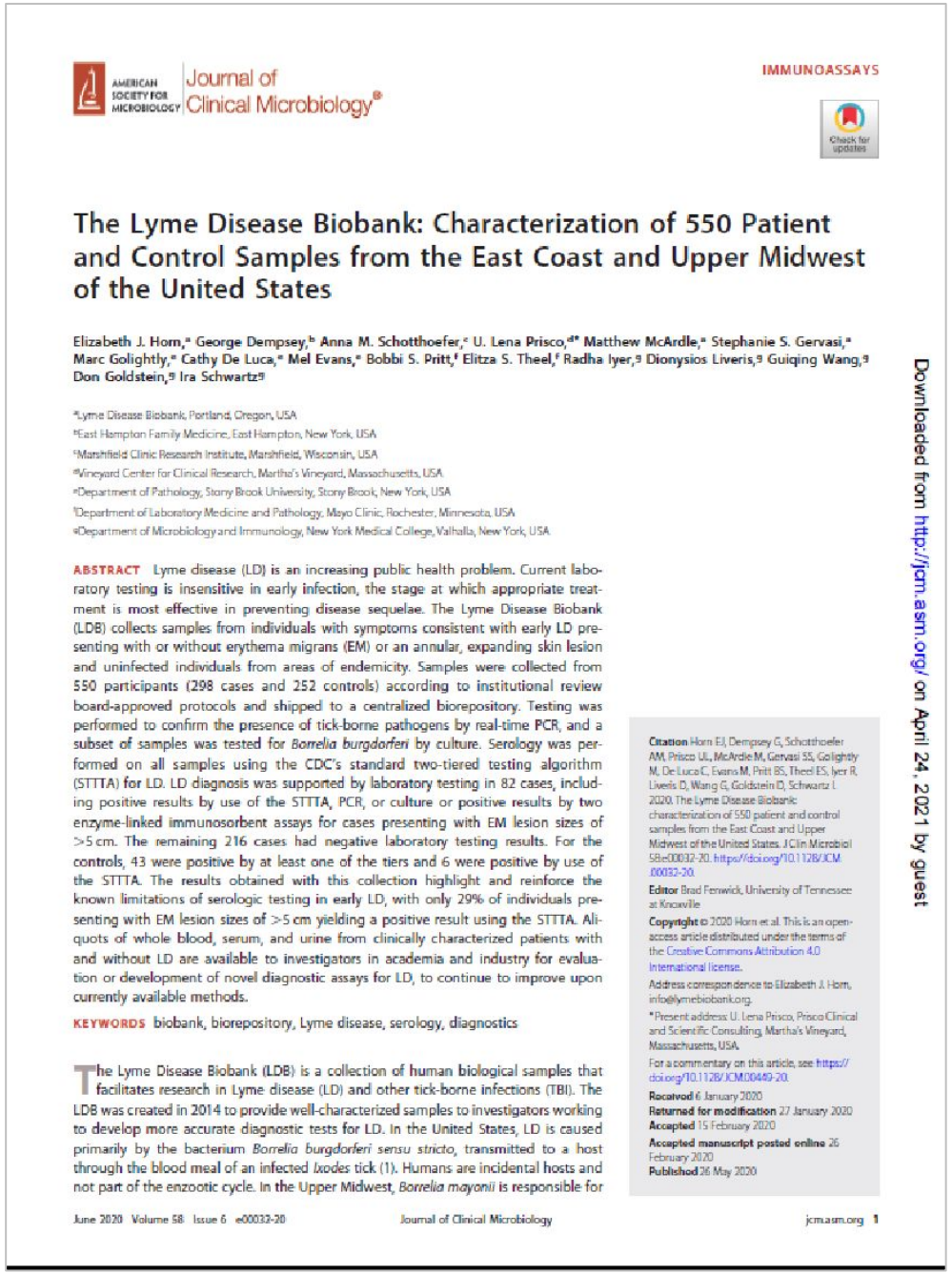
Number of cases of notifiable vector-borne diseases in the U.S. in 2018, by disease

Number of cases of vector-borne disease U.S. 2018, by disease



Note(s): United States
Further information regarding this statistic can be found on page 8.
Source(s): CDC (NNDSS); ID 742326

statista



Journal of Clinical Microbiology®

IMMUNOASSAYS

The Lyme Disease Biobank: Characterization of 550 Patient and Control Samples from the East Coast and Upper Midwest of the United States

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ABSTRACT Lyme disease (LD) is an increasing public health problem. Current laboratory testing is insensitive in early infection, the stage at which appropriate treatment is most effective in preventing disease sequelae. The Lyme Disease Biobank (LDB) collects samples from individuals with symptoms consistent with early LD presenting with or without erythema migrans (EM) or an annular, expanding skin lesion and uninfected individuals from areas of endemicity. Samples were collected from 550 participants (298 cases and 252 controls) according to institutional review board-approved protocols and shipped to a centralized biorepository. Testing was performed to confirm the presence of tick-borne pathogens by real-time PCR, and a subset of samples was tested for *Borrelia burgdorferi* by culture. Serology was performed on all samples using the CDC's standard two-tiered testing algorithm (STTTA) for LD. LD diagnosis was supported by laboratory testing in 82 cases, including positive results by use of the STTTA, PCR, or culture or positive results by two enzyme-linked immunosorbent assays for cases presenting with EM lesion sizes of >5 cm. The remaining 216 cases had negative laboratory testing results. For the controls, 43 were positive by at least one of the tiers and 6 were positive by use of the STTTA. The results obtained with this collection highlight and reinforce the known limitations of serologic testing in early LD, with only 29% of individuals presenting with EM lesion sizes of >5 cm yielding a positive result using the STTTA. Aliquots of whole blood, serum, and urine from clinically characterized patients with and without LD are available to investigators in academia and industry for evaluation or development of novel diagnostic assays for LD, to continue to improve upon currently available methods.

KEYWORDS biobank, biorepository, Lyme disease, serology, diagnostics

The Lyme Disease Biobank (LDB) is a collection of human biological samples that facilitates research in Lyme disease (LD) and other tick-borne infections (TBI). The LDB was created in 2014 to provide well-characterized samples to investigators working to develop more accurate diagnostic tests for LD. In the United States, LD is caused primarily by the bacterium *Borrelia burgdorferi sensu stricto*, transmitted to a host through the blood meal of an infected *Ixodes* tick (1). Humans are incidental hosts and not part of the enzootic cycle. In the Upper Midwest, *Borrelia mayonii* is responsible for

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Editor Brad Fenwick, University of Tennessee at Knoxville

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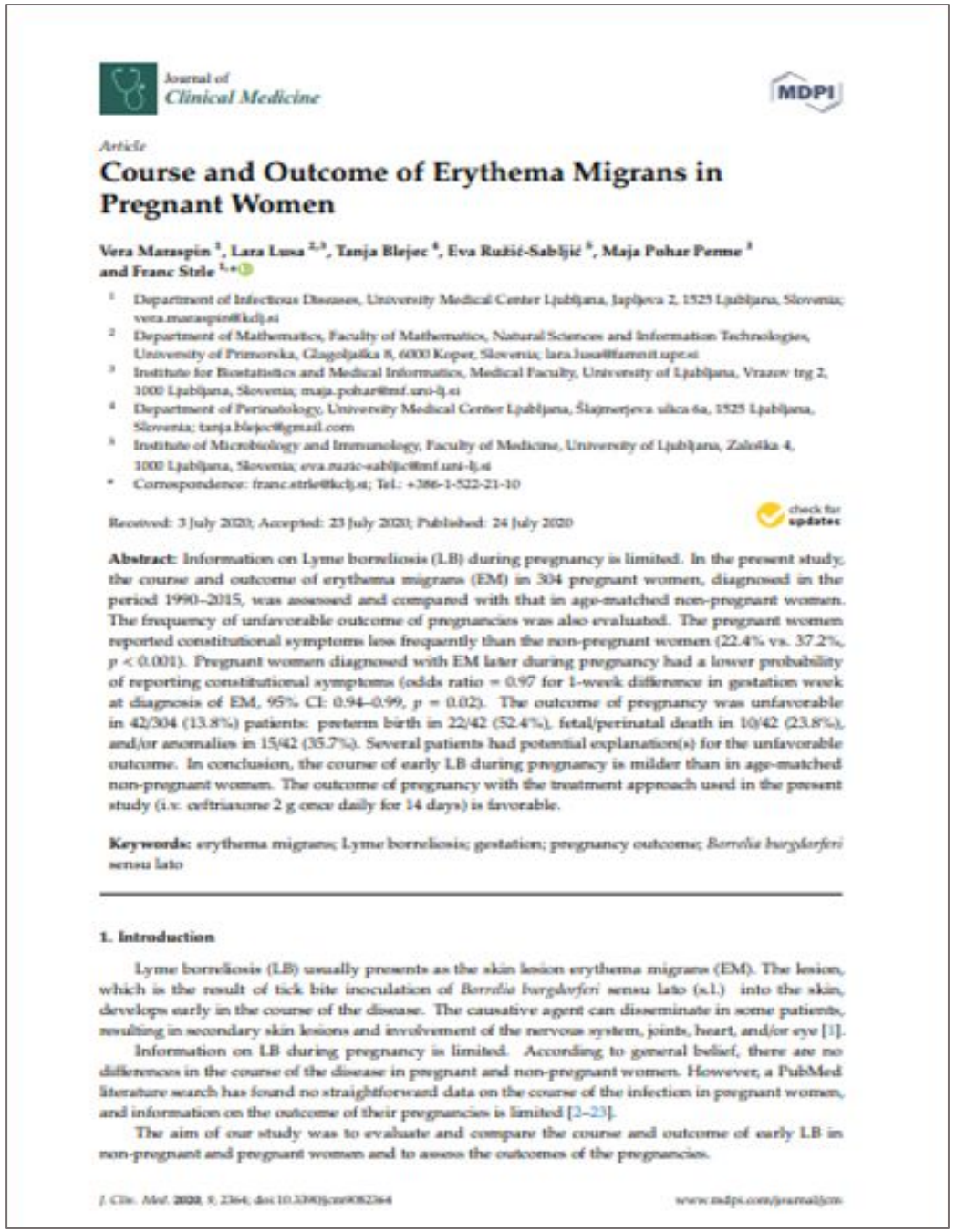
- "A lack of provider awareness of the ***absence of EM or nonclassical EM presentations can lead to underdiagnosis and delayed treatment***, highlighting the need for better diagnostics for early LD."

- "Insufficiencies in current testing methodologies ***complicate the accurate diagnosis of early LD, contribute to delays in diagnosis and treatment***, and may result in additional sequelae."

- The results obtained with this collection highlight and ***reinforce the known limitations of serologic testing in early LD***, with ***only 29% of individuals*** presenting with EM lesion sizes of >5 cm yielding a positive result using the STTTA.



Journal of Clinical Medicine

MDPI

Article

Course and Outcome of Erythema Migrans in Pregnant Women

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Abstract: Information on Lyme borreliosis (LB) during pregnancy is limited. In the present study, the course and outcome of erythema migrans (EM) in 304 pregnant women, diagnosed in the period 1990–2015, was assessed and compared with that in age-matched non-pregnant women. The frequency of unfavorable outcome of pregnancies was also evaluated. The pregnant women reported constitutional symptoms less frequently than the non-pregnant women (22.4% vs. 37.2%, $p < 0.001$). Pregnant women diagnosed with EM later during pregnancy had a lower probability of reporting constitutional symptoms (odds ratio = 0.97 for 1-week difference in gestation week at diagnosis of EM, 95% CI: 0.94–0.99, $p = 0.02$). The outcome of pregnancy was unfavorable in 42/304 (13.8%) patients: preterm birth in 22/42 (52.4%), fetal/perinatal death in 10/42 (23.8%), and/or anomalies in 15/42 (35.7%). Several patients had potential explanation(s) for the unfavorable outcome. In conclusion, the course of early LB during pregnancy is milder than in age-matched non-pregnant women. The outcome of pregnancy with the treatment approach used in the present study (i.v. ceftriaxone 2 g once daily for 14 days) is favorable.

Keywords: erythema migrans; Lyme borreliosis; gestation; pregnancy outcome; *Borrelia burgdorferi* sensu lato

1. Introduction

Lyme borreliosis (LB) usually presents as the skin lesion erythema migrans (EM). The lesion, which is the result of tick bite inoculation of *Borrelia burgdorferi* sensu lato (s.l.) into the skin, develops early in the course of the disease. The causative agent can disseminate in some patients, resulting in secondary skin lesions and involvement of the nervous system, joints, heart, and/or eye [1].

Information on LB during pregnancy is limited. According to general belief, there are no differences in the course of the disease in pregnant and non-pregnant women. However, a PubMed literature search has found no straightforward data on the course of the infection in pregnant women, and information on the outcome of their pregnancies is limited [2–23].

The aim of our study was to evaluate and compare the course and outcome of early LB in non-pregnant and pregnant women and to assess the outcomes of the pregnancies.

"***Pregnant woman women less often had a ring-like EM*** (42.4% vs. 55.3%, $p = 0.002$), less often had EM located on the trunk (14.1% vs. 24.0%, $p = 0.009$), and ***less often reported constitutional symptoms*** (22.4% vs. 37.2%, $p < 0.001$)."

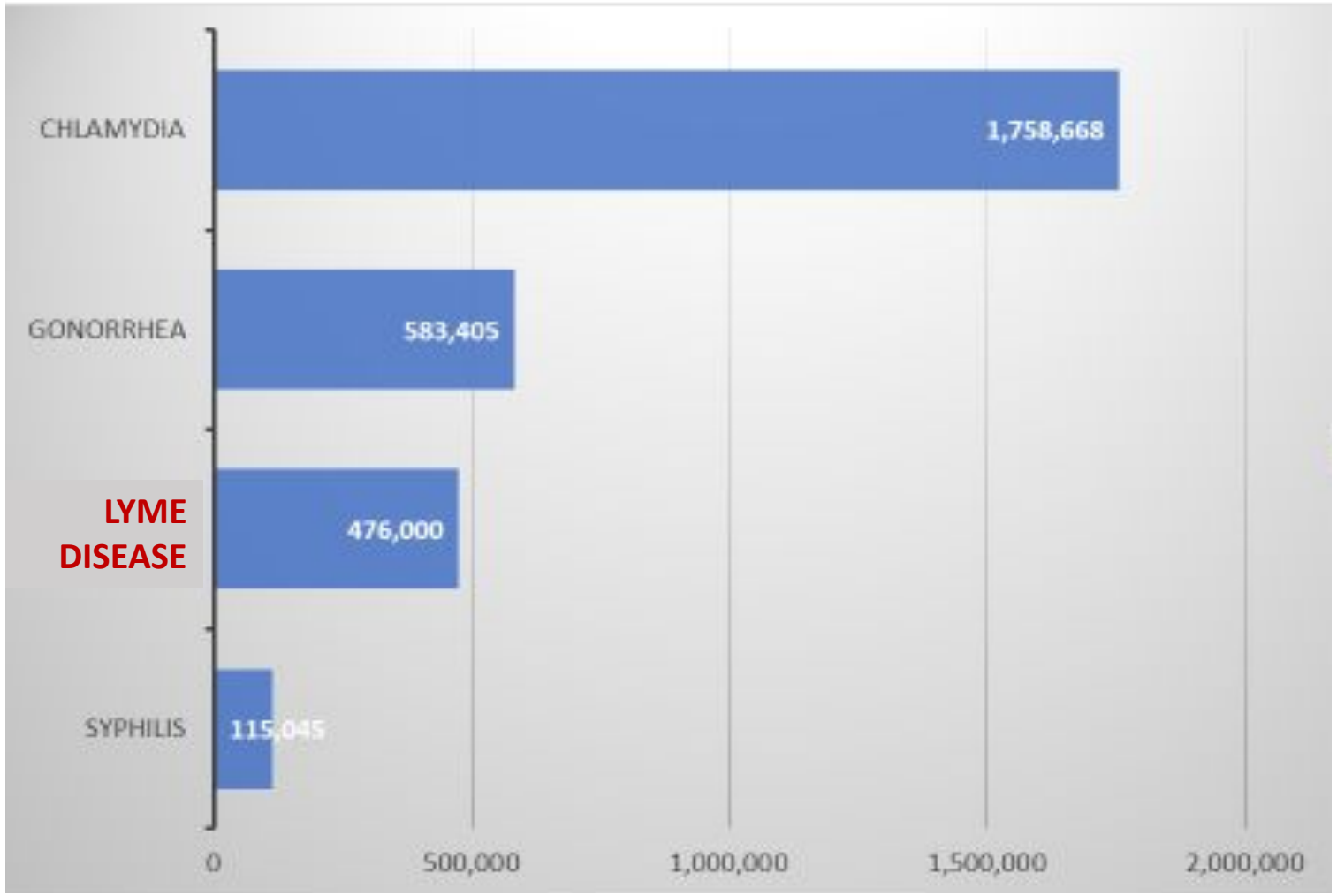
"We do not have a reliable explanation for the observation that the pregnant women less often had ring-like EM despite similar duration of the skin lesion before treatment, ***but we stress that the findings in our control group are in agreement with previous reports.***"

"Most manifestations of LB result from inflammation generated by the host immune response to the spirochete. ***Thus, fewer symptoms, as found in the present study of pregnant women with EM, may be associated with lower levels of inflammation.***

https://www.cdc.gov/lyme/stats/humancases.html

*"A recently released estimate based on insurance records suggests that **each year approximately 476,000 Americans** are diagnosed and treated for Lyme disease."*

Comparing Annual Cases of STDs to Lyme disease

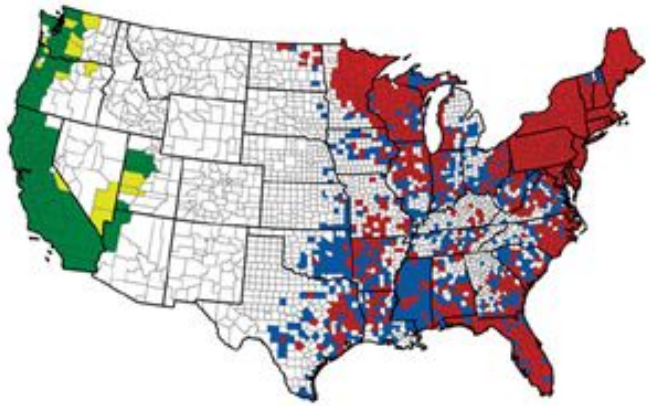


https://www.cdc.gov/nchs/hus/contents2019.htm#Table-010

Considerations

- Case numbers of other vector-borne diseases show that ticks are not great vectors.
- Distribution of vectors in US:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4844559/



- Data strongly suggests ***other routes of transmission***
- Data also suggests ***humans have become reservoir hosts***

VECTOR-BORNE AND ZOONOTIC DISEASES
Volume 15, Number 11, 2015

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REVIEW

Congenital Tick Borne Diseases: Is This An Alternative Route of Transmission of Tick-Borne Pathogens In Mammals?

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Abstract

Tick-borne diseases (TBDs) have become a popular topic in many medical journals. Besides the obvious participation of ticks in the transmission of pathogens that cause TBD, little is written about alternative methods of their spread. An important role is played in this process by mammals, which serve as reservoirs. Transplacental transfer also plays important role in the spread of some TBD etiological agents. Reservoir species take part in the spread of pathogens, a phenomenon that has extreme importance in synanthropic environments. Animals that accompany humans and animals migrating from wild lands to urban areas increase the probability of pathogen infections by ticks This article provides an overview of TBDs, such as tick-borne encephalitis virus (TBEV), and TBDs caused by spirochetes, α-proteobacteria, γ-proteobacteria, and Apicomplexa, with particular attention to reports about their potential to cross the maternal placenta. For each disease, the method of propagation, symptoms of acute and chronic phase, and complications of their course in adults, children, and animals are described in detail. Additional information about transplacental transfer of these pathogens, effects of congenital diseases caused by them, and the possible effects of maternal infection to the fetus are also discussed. The problem of vertical transmission of pathogens presents a new challenge for medicine. Transfer of pathogens through the placenta may lead not only to propagation of diseases in the population, but also constitute a direct threat to health and fetal development. For this reason, the problem of vertical transmission requires more attention and an estimation of the impact of placental transfer for each of listed pathogens.

Key Words: Tick-borne diseases—Congenital diseases—Transplacental transmission.

Introduction

During the last 30 years, much attention has been paid to diseases transmitted by ticks—tick-borne diseases (TBDs). There is an extensive literature describing this issue, usually epidemiologically, and drawing attention to the methods of how the various pathogens are spread. Ticks function as vectors, but animals that are their reservoirs play an important role as well. Many publications describe the phenomenon of pathogen transfer between vectors—ticks—which can be done by co-feeding and vertically by germ cells.

Relatively few publications describe cases of pregnant mother and newborn infections, pointing out another possibility of TBD pathogens spread by penetration through the placenta of infected animals and humans, in other words, the possibility of intergenerational infection. A properly developed placenta is supposed to be a selective barrier through which, theoretically, no pathogens should cross. However, this is not true. Clinical observations have provided information about etiological factors of congenital diseases that cross the placental barrier, thus confirming the transplacental transmission of such pathogens as viruses, bacteria, and protozoa (Robbins and Bakardjiev 2012).

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[2]University of Silesia in Katowice, Faculty of Computer Science and Material Science, Institute of Material Science, Katowice, Poland.
[3]Provincial Sanitary and Epidemiological Station in Katowice, Katowice, Poland.
[4]Department of Animal Histology and Embryology, University of Silesia in Katowice, Faculty of Biology and Environmental Protection, Katowice, Poland.

"Despite the fact that some authors consider that antibiotic therapy of a pregnant mother diagnosed with Lyme disease allows normal development of the child (Walsh et al. 2007, Leslein 2010), it must be kept in mind that the treatment of Lyme disease is sometimes long and difficult (Embers et al. 2012). ***The ability of long-term survival of B. burgdorferi in tissues and spreading of spirochetes in the body despite antibiotic treatment can contribute to intergenerational infection of Lyme disease***."

Animal Studies Showing Vertical Transmission of *Borrelia burgdorferi*

1	Anderson JF, Johnson RC, Magnarelli LA. Seasonal prevalence of Borrelia burgdorferi in natural populations of white- footed mice, Peromyscus leucopus. Journal of Clinical Microbiology, Vol 25(8)Aug, 1987, p. 1564-1566.
2	Experimental and epizootiologic studies of Lyme disease Ubico-Navas, Sonya Renee, Ph.D. Colorado State University, 1992.
3	Burgess EC, Wachal MD, Cleven TD. Borrelia burgdorferi infection in dairy cows, rodents, and birds from four Wisconsin dairy farms. Vet Microbiol. 1993 May;35(1-2):61-77. doi: 10.1016/0378-1135(93)90116-o. PMID: 8362496.
4	Silver RM, Yang L, Daynes RA, Branch DW, Salafia CM, Weis JJ. Fetal outcome in murine Lyme disease. *Infect Immun*. 1995;63(1):66-72. doi:10.1128/IAI.63.1.66-72.1995
5	Altaie SS, Mookherjee S, Assian E, Al-Taie F, Nakeeb SM, Siddiqui SY. Transplacental transmission of Bb in a Murine Model. 10th Annual International Scientific Conference on Lyme Disease and other Tick-Borne Disorders, National Institutes of Health, Bethesda MD April 28-30, 1997.
6	Hou X. [Preliminary investigation on reservoir hosts of Borrelia burgdorferi in China]. Wei Sheng Yan Jiu. 1999 Jan 30;28(1):7-9. Chinese. PMID: 12712735.
7	Burgess EC. Borrelia burgdorferi infection in Wisconsin horses and cows. Ann N Y Acad Sci. 1988;539:235-43. doi: 10.1111/j.1749-6632.1988.tb31857.x. PMID: 3190095.
8	Leibstein MM, Khan MI, Bushmich SL. Evidence for in-utero Transmission of Borrelia burgdorferi from Naturally Infected Cows. Journal of Spirochetal and Tick-borne Diseases. Vol 5, Fall/Winter, 1998: 54-62.
9	Burgess EC, Gendron-Fitzpatrick A, Mattison M. Foal mortality associated with natural infection of pregnant mares with Borrelia burgdorferi. In Proceedings, 5th Int Conf Equine Infectious Dis, 1989, 217-220.
10	Gustafson, John Michael, Ph.D. The in utero and seminal transmission of Borrelia burgdorferi in Canidae. The University of Wisconsin - Madison, 1993. PhD Thesis.
11	Gustafson JM, Burgess EC, Wachal MD, Steinberg H. Intrauterine transmission of Borrelia burgdorferi in dogs. Am J Vet Res. 1993 Jun;54(6):882-90.
12	Burgess EC, Windberg LA. Borrelia SP. Infection in coyotes, black-tailed Jack rabbits and desert cottontails in Southern Texas. Journal of Wildlife Diseases 25(1), 1989, pp. 47-51.

"It is possible that ***non-arthropod transmission could introduce the spirochete into populations outside of the geographical range of the tick vector***. The apparent ease by which organisms can be transmitted by these mechanisms demands closer inspection if the overall epidemiologic and epizootiologic picture is to be understood." – Gustafsen, 1993

"If ***fetuses can be infected in-utero with B. burgdorferi, as suggested by Anderson et al.*** (1987), and if they can survive transplacental transmission, this may be **a** means of maintaining the spirochete in the rodent population in the absence of ticks." – Burgess, 1993

"… these results indicated ***that B. burgdorferi can transmit by other modes than the tick bite***." – Altaie et al, 1996

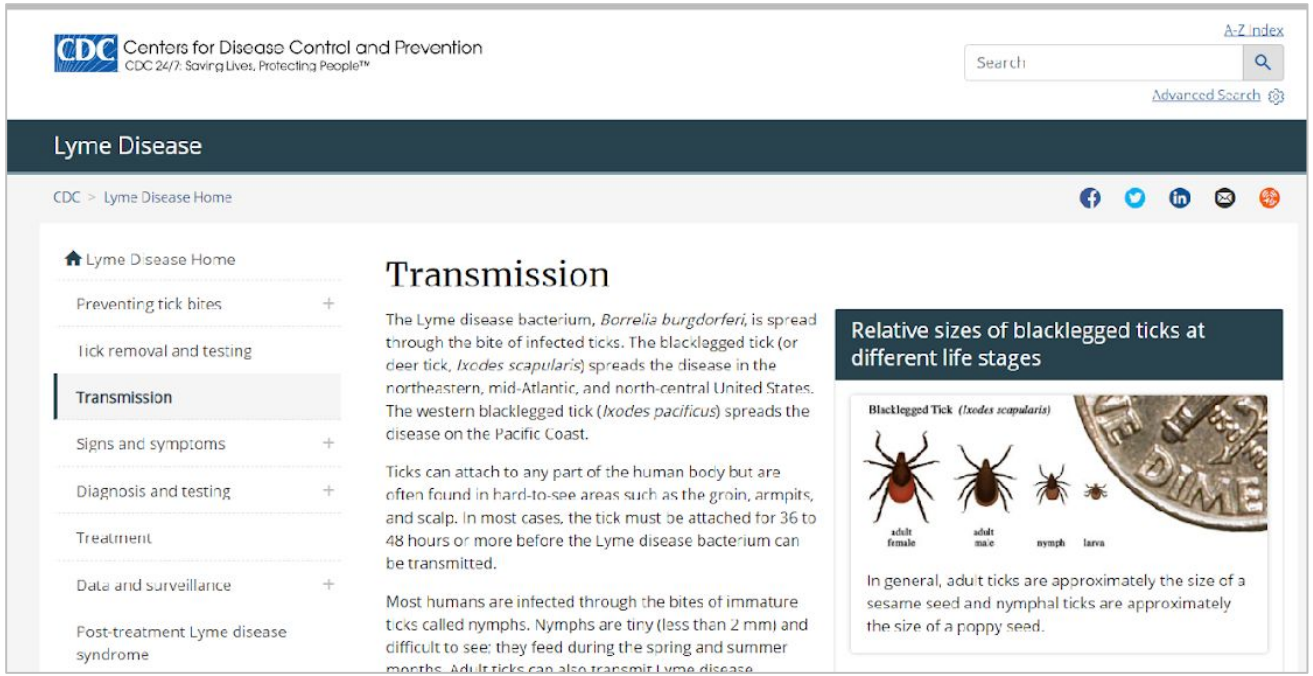
"This could mean that a survey for Bb infection using the presence of antibodies alone as the method of detection may underestimate the prevalence of infection." – Burgess et al, 1989.

"Intrauterine infection by *B. burgdorferi* does occur in dogs and is a potential means by which ***the spirochete can be transmitted in a breeding population in the absence of a tick vector***." – Gustafson et al, 1993

"The findings of this study of natural *B. burgdorferi* infection in pregnant dairy heifers supports previous observations of both natural and experimental in-utero infections with *B. burgdorferi* in domestic animals and ***give further evidence of B. burgdorferi occurs during gestation*** in naturally infected cattle." – Bushmich et al, 1998

"Vertical transmission of *B. burgdorferi* was confirmed with *B. burdorferi* isolated from foetuses of *Apodemus agrarius* and *Rattus edwardsi*. ***The results showed that Lyme disease spirochetes might be naturally maintained in an enzootic cycle by transplacental transmission***." - Wan et al, 1999.

CDC 2020



Are there other ways to get Lyme disease?

- "Untreated Lyme disease during pregnancy *can lead to infection of the placenta. Spread from mother to fetus is possible but rare*.
- *Fortunately, with appropriate antibiotic treatment, there is no increased risk of adverse birth outcomes*.
- *There are no published studies assessing developmental outcomes of children whose mothers acquired Lyme disease during pregnancy."*

CDC 1985

Current Trends Update: Lyme Disease and Cases Occurring during Pregnancy -- United States

MMWR June 28, 1985 / 34(25);376-8,383-4

"…CDC have ***established a registry*** to enroll cases of Lyme disease in pregnant women before the outcome of pregnancy is known. Of the ***19 pregnancies*** evaluated to date, none resulted in a child with a congenital heart defect. ***However, other adverse outcomes were found, including intrauterine fetal demise in the second trimester, prematurity, and developmental delay with cortical blindness.*** None of the adverse outcomes have been documented to be caused by Lyme disease. ***Outcomes of 14 of the pregnancies were completely normal.*** The risk of adverse outcome for pregnancies complicated by Lyme disease is not currently known.

5 of 19 (26%) pregnancies had adverse outcomes

Adverse fetal outcomes in pregnant moms with Lyme disease

"…appraised by fetal loss and stillbirth, pre-term birth, offspring malformations…"

2010

"Adverse outcomes" in **12%** of **IV treated moms**; **31.6%** of **oral treated moms**; and **60%** of **untreated moms**

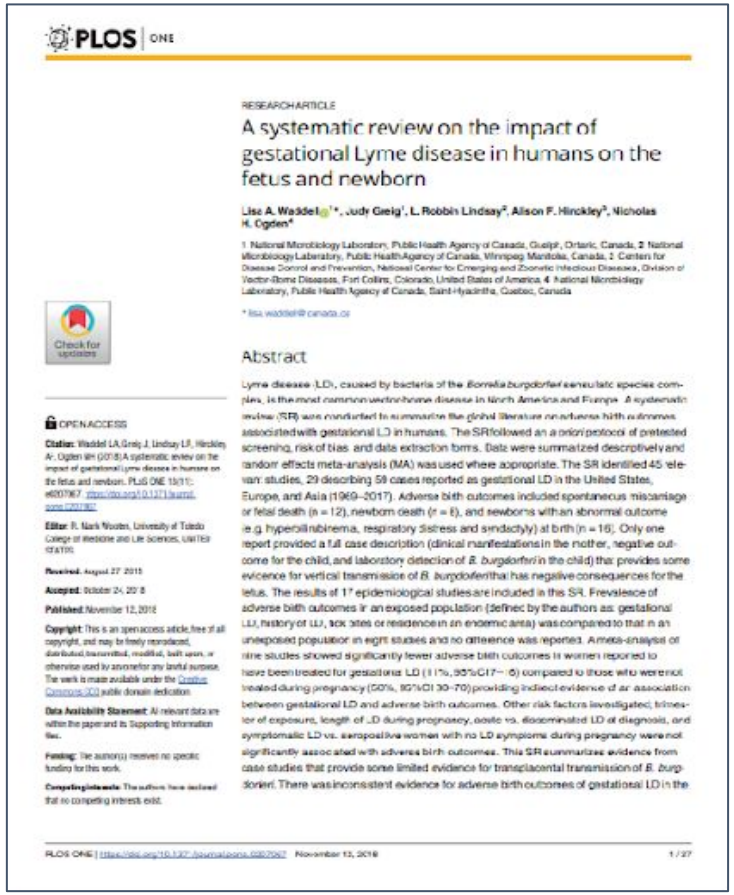
International Journal of Infectious Diseases

Maternal Lyme borreliosis and pregnancy outcome

András Lakos [a,*], Norbert Solymosi [b]

2018

"Adverse outcomes" in **11%** of **treated** moms and **50%** of **untreated moms**



PLOS ONE

RESEARCH ARTICLE

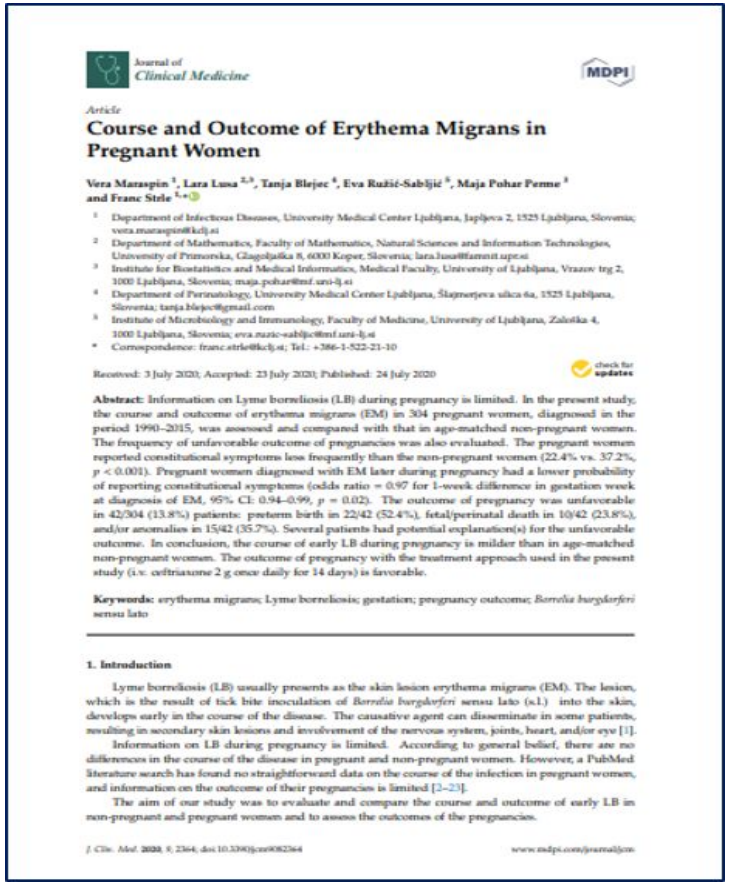
A systematic review on the impact of gestational Lyme disease in humans on the fetus and newborn

Lisa A. Waddell[1]*, Judy Greig[1], L. Robbin Lindsay[2], Alison F. Hinckley[3], Nicholas H. Ogden[4]

Abstract

2020

"Adverse outcomes" in **14%** of IV treated moms. All pregnant moms were treated



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Article

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Vera Maraspin [1], Lara Lusa [2,3], Tanja Blejec [4], Eva Ružić-Sabljić [5], Maja Pohar Perme [3] and Franc Strle [1,*]

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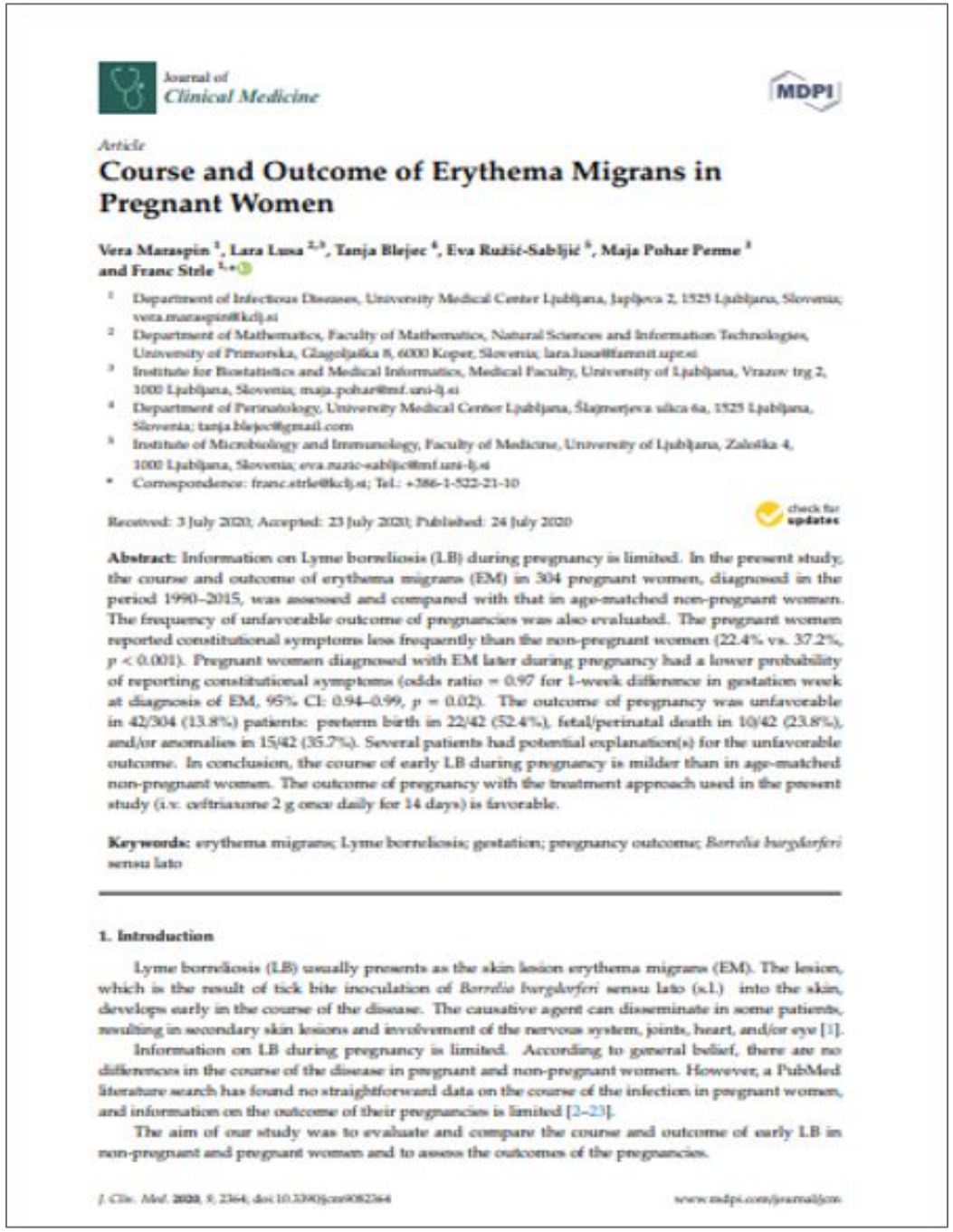

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Keywords: erythema migrans; Lyme borreliosis; gestation; pregnancy outcome; *Borrelia burgdorferi* sensu lato

1. Introduction

Lyme borreliosis (LB) usually presents as the skin lesion erythema migrans (EM). The lesion, which is the result of tick bite inoculation of *Borrelia burgdorferi* sensu lato (s.l.) into the skin, develops early in the course of the disease. The causative agent can disseminate in some patients, resulting in secondary skin lesions and involvement of the nervous system, joints, heart, and/or eye [1].

Information on LB during pregnancy is limited. According to general belief, there are no differences in the course of the disease in pregnant and non-pregnant women. However, a PubMed literature search has found no straightforward data on the course of the infection in pregnant women, and information on the outcome of their pregnancies is limited [2–23].

The aim of our study was to evaluate and compare the course and outcome of early LB in non-pregnant and pregnant women and to assess the outcomes of the pregnancies.

"In conclusion, the course of early LB during pregnancy is **milder than in age-matched non-pregnant women**. The ***outcome of pregnancy*** with the treatment approach used in the present study (i.v. ceftriaxone 2 g once daily for 14 days*) is* ***favorable***."

The outcome of pregnancy was ***unfavorable in 42/304 (13.8%) of TREATED patients***

- Preterm birth in 22/42 (52.4%)
- Fetal/perinatal death in 10/42 (23.8%)
- Anomalies in 15/42 (35.7%).

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Syphilis and borreliosis during pregnancy

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ABSTRACT: Syphilis and lyme borreliosis have similar etiologic, clinical, and epidemiologic characteristics. Both are multisystem infectious disorders spread worldwide. Their clinical course can be divided into three stages and as to spirochetal origin, antibiotic therapy is similar too. Taxonomical relationship of *Treponema* and *Borrelia* could explain also congenital manifestations well-known in syphilis, and suggested in borreliosis. Therapy of pregnant women with syphilis and lyme borreliosis should follow the same strategy.

KEYWORDS: borrelia burgdorferi, lyme borreliosis, pregnancy, syphilis, treponema pallidum

Introduction

Syphilis is a multisytem infectious disease caused by *Treponema pallidum* acquired by sexual contact, it is a classical sexually transmitted disease distributed worldwide. Lyme borreliosis is a multisystem infectious disease caused by *Borrelia burgdorferi* sensu lato transmitted by ticks, it is the most frequent anthropozoonosis distributed worldwide too. Both, *Treponema* and *Borrelia* belong to the order Spirochetales that are pathogenic to humans (1).

T. pallidum measures 12 μm in length and 0.15 μm in width. It has 8–10 coils on average, moves by rotation and flexes centrally. Its replication time is 33 hours. Syphilis is most frequent in people with a high sexual activity. Despite being reported worldwide, primary and secondary stages of the disease remain a problem, but tertiary and congenital syphilis have decreased in Western countries. On the contrary, they could significantly increase perinatal mortality rate in underdeveloped countries, including previous countries of the Soviet block (2). Another problem is an association of syphilis with other sexually transmitted infections, i.e., hepatitis B and C and HIV positivity. Syphilis infection in children is mainly caused by transplacental transmission; the infection during labor is not proved.

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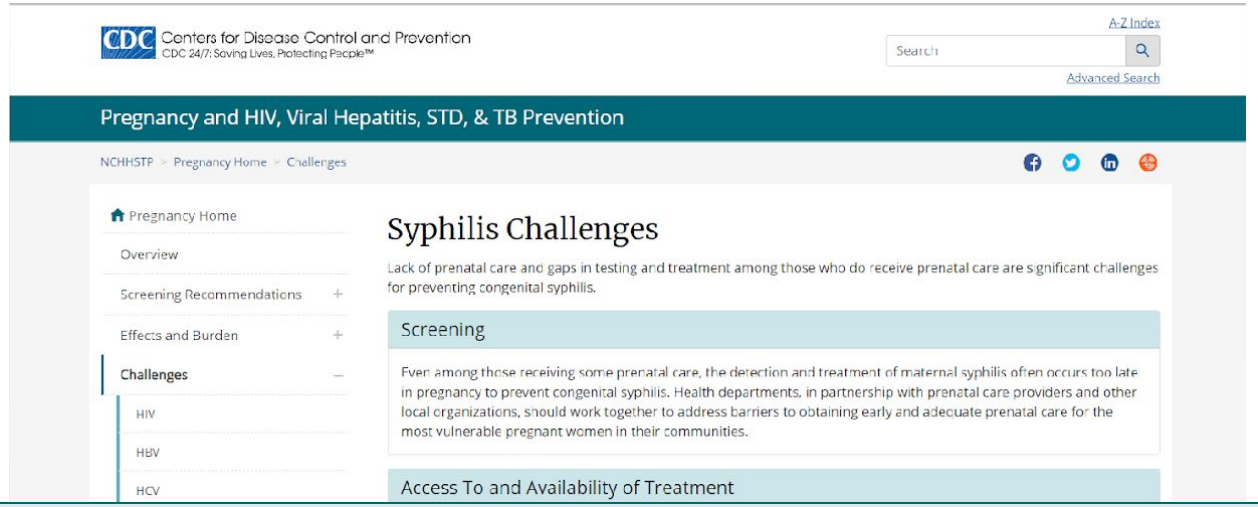
Syphilis course is divided into three stages – primary, secondary, and tertiary. The typical ulcus durum lesion appears at the site of inoculation after approximately 3 weeks. Atypical clinical pictures of chancre are increasing, they can be present as multiple lesions with crust and tenderness. Firm and nontender enlargement of regional lymph nodes follows, and spontaneous healing occurs within 4–6 weeks. Six weeks later, secondary syphilis begins in 30–40% of untreated patients. It is caused by hematogenous spread of *T. pallidum* and it could involve all body organs. The main symptoms are generalized lymphadenopathy, influenza-like symptoms (headache, upper respiratory symptoms, pharyngitis, malaise, hepatospenomegaly, etc.), mucocutaneous lesions (roseola syphiliticum, papulosquamous lesion on palms and soles, hypertrophic moist papule – condylomata lata, enanthems, alopecia, etc.). Tertiary syphilis occurs in one of six patients with untreated secondary syphilis. It could be neurosyphilis (6.5%), cardiovascular disease (10.5%), other (2%), and in 10.8% syphilis can be the primary cause of death (1).

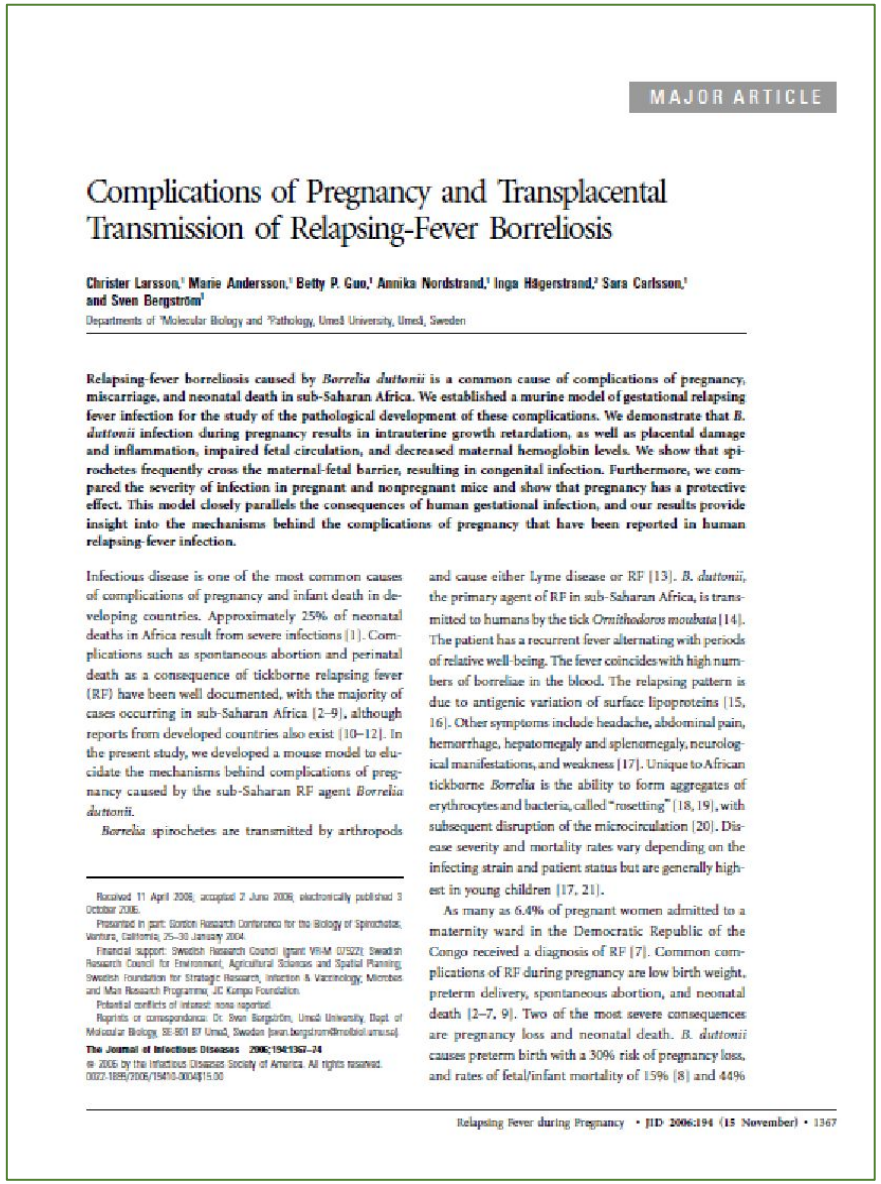
B. burgdorferi measures 10–30 μm in length and 0.2–0.3 μm in width. It has 3–10 coils on average, moves by rotation and flexes centrally. Its replication time is 7–20 hours. Borreliosis is an infection of animals (rodents, deers, pigs, birds, etc.), transmitted to humans by *Ixodes* ticks. Its incidence varies according to the occurrence of infected animals and vectors. Despite being reported worldwide,

"Several spirochetes are known to cause transplacental infections in animals and humans. *T. pallidum* is the spirochete that has been the most known to cause congenital infection in humans. Adverse fetal outcomes have also been reported in gestational infections with *Leptospira canicola*, the etiologic agent of leptospirosis, and with *Borrelia* species including *Borrelia recurrentis*, the etiologic agent of relapsing fever (6). *B. burgdorferi* is a spirochete, thus congenital infection could be predicted."



- Lack of prenatal care and ***gaps in testing and treatment*** among those who do receive prenatal care are significant challenges for preventing congenital syphilis.
- Even among those receiving some prenatal care, ***the detection and treatment of maternal syphilis often occurs too late in pregnancy to prevent congenital syphilis***.

Broaden the perspective to “Borreliosis” not just Lyme borreliosis?



MAJOR ARTICLE

Complications of Pregnancy and Transplacental Transmission of Relapsing-Fever Borreliosis

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Relapsing-fever borreliosis caused by *Borrelia duttonii* is a common cause of complications of pregnancy, miscarriage, and neonatal death in sub-Saharan Africa. We established a murine model of gestational relapsing fever infection for the study of the pathological development of these complications. We demonstrate that *B. duttonii* infection during pregnancy results in intrauterine growth retardation, as well as placental damage and inflammation, impaired fetal circulation, and decreased maternal hemoglobin levels. We show that spirochetes frequently cross the maternal-fetal barrier, resulting in congenital infection. Furthermore, we compared the severity of infection in pregnant and nonpregnant mice and show that pregnancy has a protective effect. This model closely parallels the consequences of human gestational infection, and our results provide insight into the mechanisms behind the complications of pregnancy that have been reported in human relapsing-fever infection.

Infectious disease is one of the most common causes of complications of pregnancy and infant death in developing countries. Approximately 25% of neonatal deaths in Africa result from severe infections [1]. Complications such as spontaneous abortion and perinatal death as a consequence of tickborne relapsing fever (RF) have been well documented, with the majority of cases occurring in sub-Saharan Africa [2–9], although reports from developed countries also exist [10–12]. In the present study, we developed a mouse model to elucidate the mechanisms behind complications of pregnancy caused by the sub-Saharan RF agent *Borrelia duttonii*.

Borrelia spirochetes are transmitted by arthropods and cause either Lyme disease or RF [13]. *B. duttonii*, the primary agent of RF in sub-Saharan Africa, is transmitted to humans by the tick *Ornithodoros moubata* [14]. The patient has a recurrent fever alternating with periods of relative well-being. The fever coincides with high numbers of borreliae in the blood. The relapsing pattern is due to antigenic variation of surface lipoproteins [15, 16]. Other symptoms include headache, abdominal pain, hemorrhage, hepatomegaly and splenomegaly, neurological manifestations, and weakness [17]. Unique to African tickborne *Borrelia* is the ability to form aggregates of erythrocytes and bacteria, called “rosetting” [18, 19], with subsequent disruption of the microcirculation [20]. Disease severity and mortality rates vary depending on the infecting strain and patient status but are generally highest in young children [17, 21].

As many as 6.4% of pregnant women admitted to a maternity ward in the Democratic Republic of the Congo received a diagnosis of RF [7]. Common complications of RF during pregnancy are low birth weight, preterm delivery, spontaneous abortion, and neonatal death [2–7, 9]. Two of the most severe consequences are pregnancy loss and neonatal death. *B. duttonii* causes preterm birth with a 30% risk of pregnancy loss, and rates of fetal/infant mortality of 15% [8] and 44%

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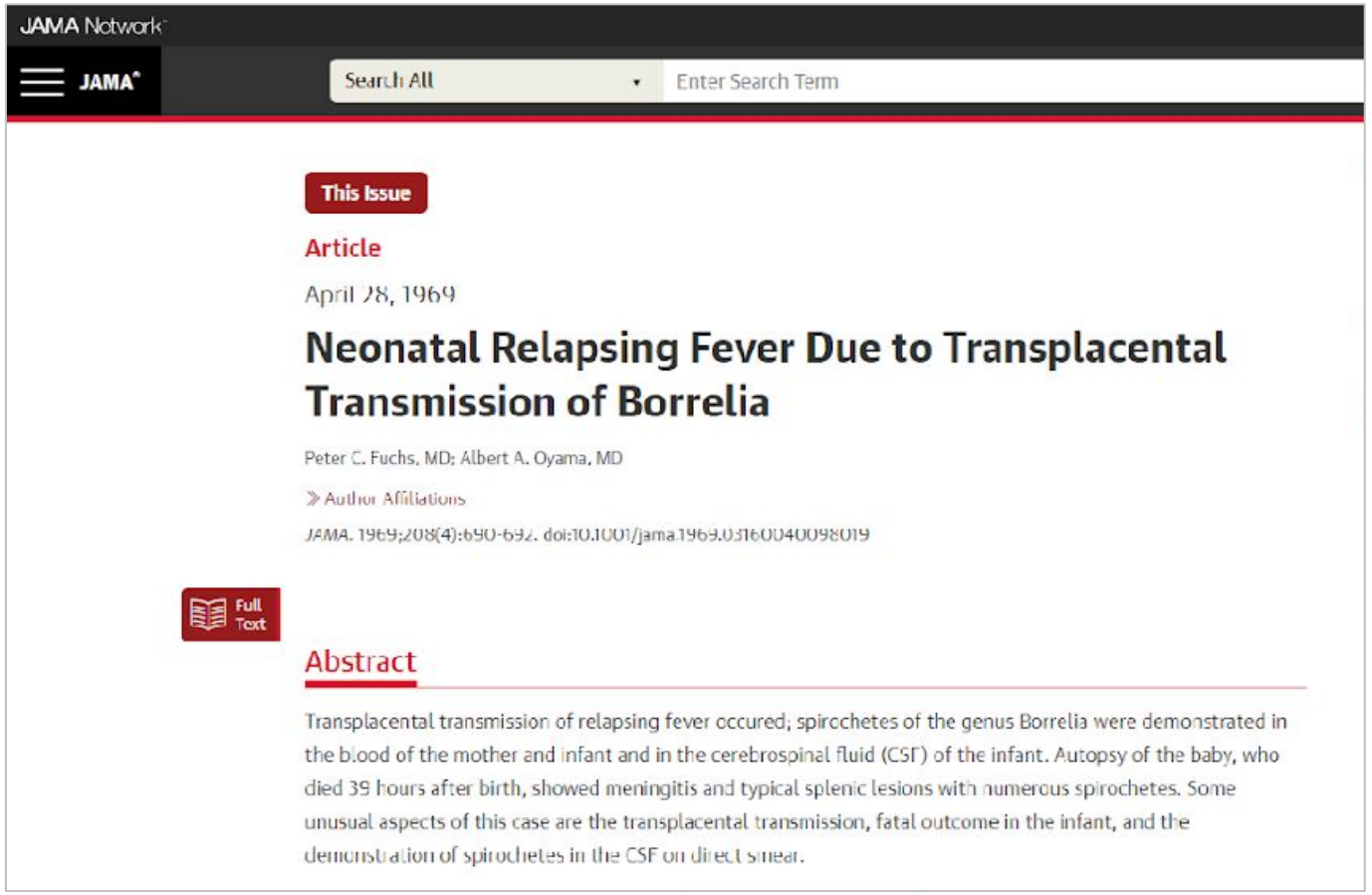

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Article

April 28, 1969

Neonatal Relapsing Fever Due to Transplacental Transmission of Borrelia

Peter C. Fuchs, MD; Albert A. Oyama, MD

» Author Affiliations

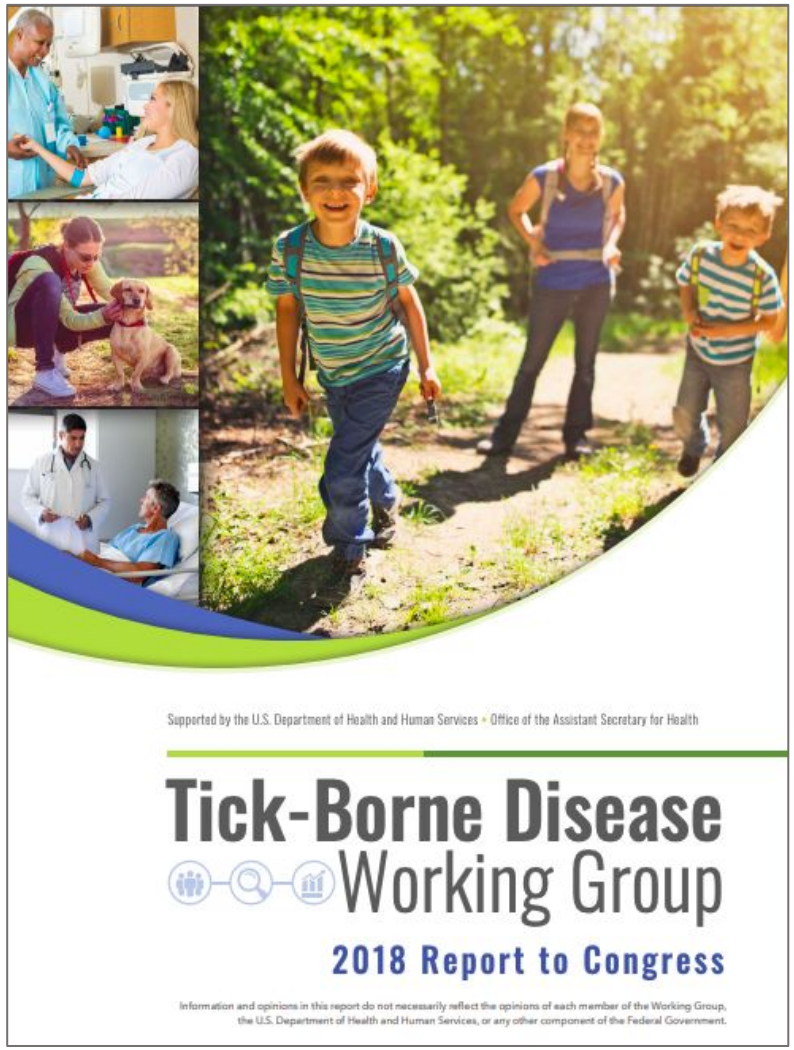
JAMA. 1969;208(4):690-692. doi:10.1001/jama.1969.03160040098019

Full Text

Abstract

Transplacental transmission of relapsing fever occured; spirochetes of the genus Borrelia were demonstrated in the blood of the mother and infant and in the cerebrospinal fluid (CSF) of the infant. Autopsy of the baby, who died 39 hours after birth, showed meningitis and typical splenic lesions with numerous spirochetes. Some unusual aspects of this case are the transplacental transmission, fatal outcome in the infant, and the demonstration of spirochetes in the CSF on direct smear.

Borrelia miyamatoi is a “relapsing fever” strain transmitted by the same ticks that transmit Lyme disease.



https://www.hhs.gov/sites/default/files/tbdwg-report-to-congress-2018.pdf

- Transplacental transmission of the human fetus has been recognized for ***relapsing fever borreliosis as well as Lyme disease…***
- Gestational tick-borne disease can be transmitted to unborn children in-utero and ***has the potential to cause premature labor and fetal death.***
- Hormonal changes during pregnancy can ***lead to changes in immune function that may affect detection of clinical or laboratory findings***.

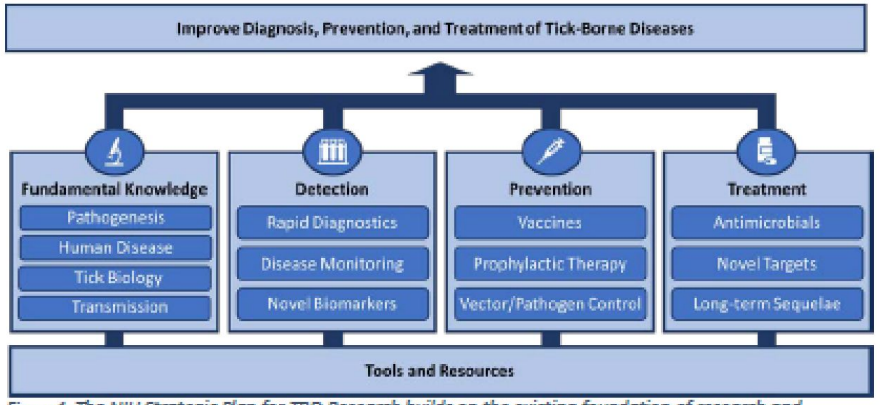


Figure 1. The NIH Strategic Plan for TBD Research builds on the existing foundation of research and resources to advance five TBD research priorities targeted at 1) improving fundamental knowledge, 2) advancing diagnosis, 3) preventing new TBD infections, 4) improving treatment for all forms of TBDs, and 5) supporting tools and resources to advance priorities 1 through 4.

2nd Report

Supported by the U.S. Department of Health and Human Services • Office of the Assistant Secretary for Health

Tick-Borne Disease Working Group

2020 Report to Congress

Information and opinions in this report do not necessarily reflect the opinions of each member of the Working Group, the U.S. Department of Health and Human Services, or any other component of the Federal government.

"Further evaluation of non-tick bite transmission of Lyme disease, for example maternal-fetal transmission."

Chapter 8

Epidemiology and Surveillance

Recommendations at a Glance: Epidemiology and Surveillance

Recommendation 8.1: Fund prospective studies of acute febrile illnesses to assess the burden of tick-borne diseases, including rickettsial, ehrlichial, and anaplasmal pathogens.

Recommendation 8.2: Recommend that CDC work with Council of State and Territorial Epidemiologists (CSTE) to streamline the surveillance process and to reduce the burden on both clinicians and public health departments by permitting direct laboratory reporting of positive cases.

Recommendation 8.3: Further evaluation of non-tick bite transmission of Lyme disease, for example maternal-fetal transmission.

https://www.hhs.gov/sites/default/files/tbdwg-2020-report_to-ongress-final.pdf

"It is surprising that the evidence presented for transplacental transmission has received little notice by investigators. It would seem that the clinical and epidemiological implications, if significant, could have an impact on current thinking and measures taken to manage the disease."

Gustafson, John Michael, Ph.D. The in utero and seminal transmission of *Borrelia burgdorferi* in Canidae. The University of Wisconsin - Madison, 1993. PhD Thesis.